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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,968	06/09/2005	George R. Pettit	12504.544	6924

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EXAMINER	
SHIAO, REI TSANG	
ART UNIT	**PAPER NUMBER**
1626	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/537,968	PETTIT ET AL.	
	Examiner	Art Unit	
	Rei-tsang Shiao, Ph.D.	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1 and 2* is/are allowed.

6)☒ Claim(s) *3 and 4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/09/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This application claims benefit of the provisional application: 60/432,219 with a filing date 12/09/2002.

2. Claims 1-4 are pending in the application.

Information Disclosure Statement

3. Applicant's Information Disclosure Statement, filed on June 09, 2005 has been considered. Please refer to Applicant's copy of the 1449 submitted herein.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using compounds of the formula of claim 3 for treating breast cancer cells, *in vitro*, it does not reasonably provide enablement for using compounds of the formula of claim 3 for treating cancer *in vivo*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described. They are:

1. the nature of the invention,

2. the state of the prior art,

3. the predictability or lack thereof in the art,

4. the amount of direction or guidance present,

5. the presence or absence of working examples,

6. the breadth of the claims,

7. the quantity of experimentation needed, and

8. the level of the skill in the art.

In the instant case:

The nature of the invention

The nature of the invention of claims 3-4 is drawn to intent methods of use using compounds of formula of claim 3 for treating cancer cells (i.e., breast cancer cells) *in vitro* or *in vivo*.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific diseases by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in

the art would prevent one of ordinary skill in the art from accepting any therapeutic or preventive regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833,166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Pettit et al. publication, Journal of Natural Products (2003), 66(1), 92-96, disclose that narcistatin and its derivatives are used for treating a number of cancer cells *in vitro*. Applicants are claiming intent methods of use using compounds of the formula of claim 3 effective to "treating a neoplatic disease" *in vitro* or *in vivo*. As such, the specification fails to enable the skilled artisan to use the compounds of claims 3-4 effective to "treating a neoplastic disease" *in vivo*.

In addition, there is no established correlation between *in vitro* activity and accomplishing treatment of "treating a neoplastic disease", *in vivo*, and those skilled in the art would not accept allegations in the instant specification to be reliable predictors of success, and those skilled in the ad would not be able to use the compounds of the formula of claim 3 since there is no description of an actual method wherein "treating a neoplastic disease" in a host is treated.

Hence, one of skill in the art is unable to fully predict possible results from the administration of the compounds of claims 3-4 due to the unpredictability of the "treating a neoplastic disease". The "treating a neoplastic disease" is known to have many

obstacles that would prevent one of ordinary skill in the art from accepting treating regimen on its face.

The amount of direction or guidance present and the presence or absence of working examples

The only direction or guidance present in the instant specification is the listing of exemplary assays, i.e., an *in vitro* assay in terms of 50% effective concentration (i.e., EC_{50} value), see page 27 of the specification. There are no *in vivo* working examples present for the treatment of a neoplastic disease by the administration of compounds of the instant invention.

The breadth of the claims

The breadth of the claims is a methods of use of the instant compounds effective to "treating a neoplastic disease" *in vitro* or *in vivo*.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what "treating a neoplastic disease" would be benefited (i.e., treated) by the administration of the instant compounds of the instant invention and would furthermore then have to determine which of the claimed methods of use would provide treatment of a neoplastic disease, if any.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which methods of use exhibit the desired pharmacological activity and which diseases would benefit from this activity. Thus, the specification fails to provide sufficient support of the broad use of the pharmaceutical compounds of the instant claims 3-4 for the "treating a neoplastic disease". As a result necessitating one of skill to perform an exhaustive search for which "treating a neoplastic disease", can be treated by what pharmaceutical compounds of the instant claims in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation, with no assurance of success. This rejection can be overcome by incorporation of the treated conditions (i.e., *in vitro*) and the named cancer cells (i.e., breast cancer cells or leukemia cells) into claims 3-4 respectively, would obviate the rejection.

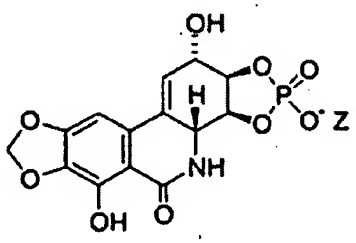
Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 3-4 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 8 and 13 of Chang et al. co-pending application No. 11/071,994. Although the conflicting claims are not identical, they are not patentably distinct from each other and reasons are as follows.

Applicants claim method of use (i.e., treating cancer) using compounds of the formula (I), i.e.,  , wherein the variable Z represents Na^+ or imidazole, see claim 3 or 4.

Chang et al. claim method of use (i.e., treating tumor metastasis) using a sodium narcistatin compound, see claim 8 or 13.

The difference between the instant claims and Chang et al. is that the instant methods of use using sodium narcistatin compound, quinidine narcistatin compound or imidazole narcistatin compound, while Chang et al. is a sodium narcistatin compound. Chang et al. methods of use overlap with the instant invention (i.e., *in vitro*).

One having ordinary skill in the art would find the instant claims 3-4 prima facie obvious **because** one would be motivated to employ the methods of use (i.e., treating cancer) uslng a sodium narcistatin compound to obtain the instant methods of use using compounds of the formula of claim 3 or 4, wherein the variable Z represents Na^+.

The motivation to obtain the claimed methods of use using compounds of claims 3-4 derives from known Chang et al. methods of use using a sodium narcistatin compound would possess similar activities (i.e., agents for treating cancer *in vitro*) to that which is claimed in the reference.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

7. Claims 1-2 are neither anticipated nor rendered obvious over the art of record, and therefore are allowable. This invention relates to narcistatin prodrug.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rei-tsang Shiao whose telephone number is (571) 272-0707. The examiner can normally be reached on 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Rei-tsang Shiao, Ph.D.
Patent Examiner
Art Unit 1626

July 30, 2007